Novel antisense therapy to treat genetic forms of neurodevelopmental disease.

Grant Award Details

Novel antisense therapy to treat genetic forms of neurodevelopmental disease.

Grant Type: Quest - Discovery Stage Research Projects

Grant Number: DISC2-13469

Project Objective: To test efficacy of antisense oligonucleotides, designed for individual patients with neurodevelopmental disorders, for restoring cellular health in patient-matched hiPSC-based neuronal models.

Investigator:

Name:	Joseph Gleeson
Institution:	University of California, San Diego
Type:	PI

Disease Focus: Autism, Epilepsy, Neurological Disorders, Other

Human Stem Cell Use: iPS Cell

Award Value: $1,180,654

Status: Active

Grant Application Details

Application Title: Novel antisense therapy to treat genetic forms of neurodevelopmental disease.

Public Abstract:

Research Objective

We propose to discovery and evaluate antisense gene therapy for specific mutations underlying debilitating or life-threatening neurodevelopmental diseases including epilepsy and autism syndromes.

Impact

The conditions are four specific neurodevelopmental syndromes where mutations are well suited to ASO therapy. The bottlenecks are current lack of cellular evidence for ASOs to impact disease course.

Major Proposed Activities

- Assemble a cohort of patients and their stem cells for study where personalized ASOs could be reasonably expected to reverse the effect of genetic mutation and lead to clinical improvement.
- Identify evidence of baseline cellular defects and gene expression defects in patient-derived stem cells from this cohort of patients.
- Design ASOs for each mutation that can correct the genetic mutation in collaboration with N Lorem Foundation.
- Assess ASO therapy for effectiveness and safety, and compare with control healthy stem cell lines.
- Deliver outcome data from this study to the PI in support of future FDA applications.

Statement of Benefit to California:

Neurodevelopmental disease impacts 1:50 Californians with conditions like severe epilepsy and autism. In prior CIRM-funded efforts we generated a library of stem cells from patients, and in parallel we identified their genetic mutations. Now the stage is set to test if correction of the genetic mutation through ASO gene therapy can show evidence of disease-modifying activity in patient cells. Results will support future clinical trials where these drugs will be administered to patients.
